

**PATENT APPLICATION**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re the Application of:

MIETTINEN et al.

Attorney Dkt. No.: 019075-00062

Application No.: Not yet assigned (Continuation of USSN 10/289,431)

Filed: Herewith

For: A SUBSTANCE FOR LOWERING HIGH CHOLESTEROL LEVEL IN SERUM AND METHODS FOR PREPARING AND USING THE SAME

**INFORMATION DISCLOSURE STATEMENT**

Commissioner for Patents  
Washington, D.C. 20231

October 6, 2003

Sir:

Pursuant to 37 CFR §1.56, the attention of the Patent and Trademark Office is hereby directed to the information items listed on the attached PTO-1449. Unless otherwise indicated herein, one copy of each item is attached. It is respectfully requested that the information be expressly considered during the prosecution of this application, and that the items be made of record therein and appear among the "References Cited" on any patent to issue therefrom.

- ☒ 1. This Information Disclosure Statement is being filed (a) within three months of the U.S. filing date, OR (b) before the mailing date of a first Office Action on the merits in the present application, OR (c) accompanies a Request for Continued Examination. No certification or fee is required.
- ☐ 2. This Information Disclosure Statement is being filed more than three months after the U.S. filing date AND after the mailing date of the first Office Action on the merits, but before the mailing date of a Final Rejection or Notice of Allowance.
- ☐ a. I hereby certify that each item of information contained in this Information Disclosure Statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Information Disclosure Statement. 37 CFR §1.97(e)(1).
- ☐ b. I hereby certify that no item of information in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application or, to my knowledge after making reasonable inquiry, was known to any individual designated in 37 CFR §1.56(c) more than three months prior to the filing of this Information Disclosure Statement. 37 CFR §1.97(e)(2).
- ☐ c. A check in the amount of \$180.00 in payment of the fee under 37 CFR §1.17(p). Please charge any fee deficiency or credit any overpayment to Deposit Account No. 01-2300 as needed to ensure consideration of the

disclosed information.

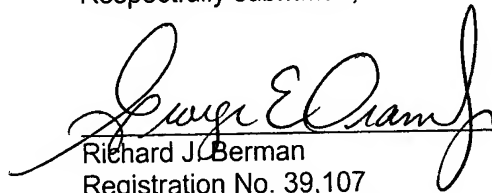
- ☐ 3. This Information Disclosure Statement is being filed more than three months after the U.S. filing date and after the mailing date of a Final Rejection or Notice of Allowance, but before payment of the Issue Fee. Applicant(s) hereby petition(s) that the Information Disclosure Statement be considered. Attached is our check in the amount of \$180.00 in payment of the petition fee under 37 CFR §1.17(i)(1). Please charge any fee deficiency or credit any overpayment to Deposit Account No. 01-2300 as needed to ensure consideration of the disclosed information.

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☐ b. I hereby certify that no item of information in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application and, to my knowledge after making reasonable inquiry, was known to any individual designated in 37 CFR §1.56(c) more than three months prior to the filing of this Information Disclosure Statement. 37 CFR §1.97(e)(2).

- ☒ 4. The reference(s) was/were cited by or submitted to the Office in parent application No. 10/289,431, filed November 7, 2002, which is relied upon for an earlier filing date under 35 U.S.C. § 120. Thus, copies of these references are not attached. 37 CFR § 1.98(d).

Respectfully submitted,

  
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<sup>1</sup>Unique citation designation number. <sup>2</sup>See attached Kinds of U.S. Patent Documents. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.1<sup>6</sup> if possible. <sup>7</sup>Applicant is to place a check mark here if English language Translation is attached.

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**LIST OF PRIOR ART CITED BY  
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(use as many sheets as necessary)

Application Number

Div. of 097713,030

Filing Date

First Named Inventor

Tatu Miettinen

Group Art Unit

Examiner Name

Sheet

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of

15

Attorney Docket Number

019075-00058

**OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS**

Examiner Initials <sup>2</sup>	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, country, where published, source.	T <sup>3</sup>
		European Journal of Clinical Investigation, Vol. 10, pp. 27-35, (1980), T. Miettinen "Phytosterolaemia, Atheromatosis and Premature Atherosclerotic Arterial Disease: A Case with High Plant Sterol Absorption, Impaired Sterol Elimination and Low Cholesterol Synthesis"	
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		Chemistry and Physics of Lipids, Vol. 15, pp. 216-221, (1975), B. Lentz, et al. "A Simple Method for the Synthesis of Cholesterol Esters in High Yield"	
		Organic Preparations and Procedures, Vol. 1(2), pp. 107-109, (1969), R. Augustine, et al. "The Palladium Catalyzed Hydrogenation of Cholesterol"	
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<b>LIST OF PRIOR ART CITED BY APPLICANT</b> (use as many sheets as necessary)		Application Number		div. of 09/713,030	
		Filing Date			
		First Named Inventor		Tatu Meitinen	
		Group Art Unit			
		Examiner Name			
Sheet	3	of	15	Attorney Docket Number 019075-00058	

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		Proc. Soc. Exp. Biol Med., Vol. 78, pp.143-147, (1951), D. Peterson "Effect of Soybean Sterols in the Diet on Plasma and Liver Cholesterol in Chicks"	
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<b>LIST OF PRIOR ART CITED BY APPLICANT</b> (use as many sheets as necessary)				Application Number	div. of 09/713,030
				Filing Date	
				First Named Inventor	Tatu Miettinen
				Group Art Unit	
				Examiner Name	
Sheet	4	of	15	Attorney Docket Number	019075-00058

## OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

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		Chemical Abstracts, Vol. 115, No. 1, (1991), T. Heinemann, et al. "Mechanisms of Action of Plant Sterols on Inhibition of Cholesterol Absorption: Comparison of Sitosterol and Sitostanol"	
		Chemical Abstracts, Vol. 112, No. 7, (1990), I. Ikeda, et al. "Effects of Sitosterol and Sitostanol and Micellar Solubility of Cholesterol"	
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		International Search Report, dated 12/11/91.	
		International Preliminary Exam Report, dated 08/04/93.	
		Copy of Written Opinion from International Preliminary Exam Authority, dated 04/14/93.	

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		Lipoprotein Metabolism, pp. 112-118, (1976), (Ed. H. Greten Berlin, Heidelberg, New York: Springer-Verlag), S. Grundy, et al. "Effects of Low Dose Phytosterols on Cholesterol Absorption in Man"	
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Application Number

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		Journal of Lipid Research, Vol. 24, pp. 1535-1544, (1993), H.T. Vanhanen, et al. "Serum Cholesterol, Cholesterol Precursors, and Plant Sterols in Hypercholesterolemic Subjects with Different apoE Phenotypes During Dietary Sitostanol Ester Treatment"	
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		European Journal of Clinical Pharmacology, Vol. 40 (Suppl.), pp. 559-563, (1991), T. Heinemann, et al. "Mechanisms of Action of Plant Sterols on Inhibition of Cholesterol Absorption"	
		The American Journal of Clinical Nutrition, Vol. 35, pp. 697-700, (1982), F. Mattson, et al. "Optimizing the Effect of Plant Sterols on Cholesterol Absorption in Man"	
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		Journal of Lipid Research, Vol. 30, pp. 1319-1330, (1989), G. Salen, et al. "Increased Sitosterol Absorption, Decreased Removal, and Expanded Body Pools Compensate for Reduced Cholesterol Synthesis in Sitosterolemia with Xanthomatosis"	

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		Journal of American Oil Chemists' Society, Vol. 54, pp. 47-50, (1977), D. Chobanov, et al. "Alterations in Glycande Composition During Interestification of Mixtures of Sunflower Oil with Lard and Tallow"	
		"Thermodynamic and Molecular Determinants of Sterol Solubilities in Bile Salt Micelles", Vol. 28, pp. 1144-1155, (1987), M. Armstrong, et al.	
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		Treatment of Severe Dyslipoproteinemia in the Prevention of Coronary Heart Disease, Vol. 4, pp. 57-59, (1993) H. Gylling, et al. "Serum Cholesterol Lowering by Dietary Simvastatin is Associated with Reduced Absorption and Synthesis of Cholesterol and Decreased Transport of LDL Apoprotein B in Men with Type II Diabetes"	
		Diabetologia, Vol. 37, pp. 773-780, (1994), H. Gylling et al. "Serum Cholesterol and Cholesterol and Lipoprotein Metabolism in Hypercholesterolemic NIDDM Patients Before and During Simvastatin Ester-Margarine Treatment"	
		Journal of Lipid Research, Vol. 36, pp. 1807-1812, (1995), H. Gylling et al. "Simvastatin Ester Margarine in Dietary Treatment of Children with Familial Hypercholesterolemia"	
		European Journal of Clinical Investigation, Vol. 23, pp. 327-331, T. Heinemann, et al. "Comparison of Intestinal Absorption of Cholesterol with Different Plant Sterols in Man"	
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FILING DATE

GROUP

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FORM PTO-1449	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. 019075-00058	SERIAL NO. Div. of 09/713,030
LIST OF REFERENCES CITED BY APPLICANT  (Use several sheets if necessary)		APPLICANT MIETTINEN, et al.	
		FILING DATE Herewith	GROUP unknown

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	BA	KOBAYASHI et al., Translation of JP 57-206336 (1982).
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	BC	VANHANEN et al., "Effects of unsaturated and saturated dietary plant sterols on their serum contents", Clinica Chimica Acta, Vol. 205, 1992, Pages 97-107.
	BD	VANHANEN et al., "Serum cholesterol, cholesterol precursors, and plant sterols in hypercholesterolemic subjects with different apoE phenotypes during dietary sitostanol ester treatment", Journal of Lipid Research, Vol. 34, 1993, Pages 1535-1544.
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	BF	Main Request - May 4, 1999 filed in the European Patent Office in European Patent No. 0 594 612 (granted on Application No. 91908435.0)
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	BK	Opposed patent as filed in Finnish; Title: A substance for lowering high cholesterol level in serum and a method for preparing the same"; Inventors: MIETTINEN et al.
	BL	Norm NEN 3428
	BM	

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		FILING DATE Herewith	GROUP unknown

**U.S. PATENT DOCUMENTS**

EXAMINER INITIAL	AA	DOCUMENT NO.	DATE	NAME	CLASS	SUB- CLASS	FILING DATE
	AA	5,244,887	09/1993	STRAUB			
	AB	4,160,850	07/1979	HALLSTROM et al.			
	AC	1,413,102	11/1975	JANDACEK			
	AD	3,852,311	12/1974	NICHOLAS et al.			

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		DOCUMENT NO.	DATE	COUNTRY	CLASS	SUB- CLASS	TRANSLATION		
							YES	NO	PART.
	AE	WO 98/06405	02/1998	PCT					
	AF	WO 96/38047	12/1996	PCT					
	AG	567,202	12/1958	CANADA					
	AH	WO 92/19640	11/1992	PCT					
	AI	967616	09/1996	ZA					
	AJ	WO 97/42830	11/1997	PCT					
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## FOREIGN PATENT DOCUMENTS

		DOCUMENT NO.	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION YES NO PART.		
	AG	EP 0 898 896 A1	03/1999	EPO					
	AH	0 203 277 A2	12/1986	EPO					

## OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)

	AM	Appeal against Decision of Opposition Division filed in the EPO on February 21, 2002 including Main Request, Opponent's schematic representation of sitosterol and sitostanol and Proprietor's schematic representation of sitostanol, sitosterol and cholesterol.
	AN	Denke, "Lack of efficacy of low-dose sitostanol therapy as an adjunct to a cholesterol-lowering diet in men with moderate hypercholesterolemia", American Journal of Clinical Nutrition, 1995, vol. 61, pages 392-396.
	AO	Swell et al., "Sterol Specificity of Pancreatic Cholesterol Esterase", Proc. Soc. Exp. Biol. Med., 1954, vol. 87, pages 216-218.
		Vahouny et al., "Absolute Requirement for Free Sterol for Absorption by Rat Intestinal Mucosa", Proc. Soc. Exp. Biol. Med., 1964, vol. 116, pages 496-498.
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DOCUMENT NO.	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
					YES NO PART.
AD	EP 0 911 385 A1	EP			
AE	JP-44-4974	2/28/44 Japan			

**OTHER REFERENCES** *(Including Author, Title, Date, Pertinent Pages, Etc.)*

AF	Page 2 of the Written Opinion of WO 92/19640
AG	Page 2 of the International Preliminary Examination Report of WO 92/19640
AH	Declaration by Ilkka Etupalta
AI	<i>Serum Plant Sterols and Cholesterol Precursors Reflect Cholesterol Absorption and Synthesis in Volunteers of a Randomly Selected Male Population</i> , Miettinen et al., Am. J. Epiderm., vol. 131, no. 1:20-31, 1990
AJ	<i>Fate of Dietary Sterols in Hydrogenated Oils and Fats</i> , P.W. Parodi, J.Am. Oil Chem. Soc., Vol. 52:345-348, 1975
AK	<i>Saturated Sterols (Stanols) in Unhydrogenated and Hydrogenated Edible Vegetable Oils and in Cereal Lipids</i> , Dutta et al., J. Sci. Food Agric., Vol. 71:383-391, 1996
AL	<i>Method for Qualitative and Quantitative Determination of Phytosterols in Vegetable Iols by LC-GC off-line</i> , Schuhmann et al., Mitt. Gebiete Lebensm. Hyg., Vol. 87:708-715, 1996
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		APPLICANT MIETTINEN et al.	
		FILING DATE October 14, 2002	GROUP

**OTHER REFERENCES** *(Including Author, Title, Date, Pertinent Pages, Etc.)*

	AO	<i>Comparison of the effects of plant sterol ester and plant stanol ester-enriched margarines in lowering serum cholesterol concentrations in hypercholesterolaemic subjects on a low-fat diet</i>
	AP	<i>Effects of Low-Fat Yogurt with Plant Stanol Esters and of Consumption Frequency on LDL-Cholesterol Levels, J. Plat et al., Summary of Presentation at 92nd AOCS Annual Meeting and Expo, May 13-16, 2001, Minneapolis, Minnesota, USA</i>
	AQ	Front page of WO 92/19640
	AR	PCT Applicant's Guide (Swedish Patent Office as ISA)
	AS	PCT Applicant's Guide (Swedish Patent Office as IPEA)
	AT	<i>Efficacy of spreads enriched with stanol-stearate esters on blood cholesterol levels, Annex I filed with the Opponent's further submissions of June 27, 2000</i>
	AU	<i>Stanol Components in Edible Fats and Oils, M. Sugano et al., Sci. Byull. Fac. Agr. Kyushu Univ., Vol. 32, no. 1:21-28, 1977</i>
	AV	<i>Ullmann's Encyclopedia of Industrial Chemistry, Vol. A16:152-153</i>
	AW	<i>Elintarvike-tekniikan Perusteet, M. Hiros et al., VAPK-kustannus, Helsinki, 1990, pages 236-241, and translation of passage bridging pages 240-241</i>
	AX	<i>Hydrogenation of sterol esters. Demonstration of hydrogenation of sterol moiety, Annex II filed with the Opponent's further submission of June 27, 2000</i>

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AH	D49, b-sitosterol, Reference list for stanols, September 6, 2002.
AI	Department of Health and Human Services, "Food Labeling: Health Claims; Plant Sterol/Stanol Esters and Coronary Heart Disease; Interim Final Rule", Federal Register, Vol. 65, No. 175, September 2000.

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